

neurons. For example, neuron N1 can send excitatory inputs to neuron N2 (*e.g.*, times  $t_1$ ,  $t_3$  and  $t_4$  in Figure 1B), and neuron N3 can send inhibitory inputs to neuron N2 (*e.g.*, time  $t_2$  in Figure 1B). The neurons receive/send excitatory and inhibitory inputs from/to a population of other neurons. The excitatory and inhibitory inputs can produce "action potentials" in the neurons, which are electrical pulses that travel through neurons by changing the flux of sodium (Na) and potassium (K) ions across the cell membrane. An action potential occurs when the resting membrane potential of the neuron surpasses a threshold level. When this threshold level is reached, an "all-or-nothing" action potential is generated. For example, as shown in Figure 1B, the excitatory input at time  $t_5$  causes neuron N2 to "fire" an action potential because the input exceeds the threshold level for generating the action potential. The action potentials propagate down the length of the axon (the long process of the neuron that makes up nerves or neuronal tracts) to cause the release of neurotransmitters from that neuron that will further influence adjacent neurons.

Figure 1C is a flowchart illustrating a method 100 for effectuating a neural-function in a patient in accordance with an embodiment of the invention. The neural-function, for example, can control a specific mental process or physiological function, such as a particular motor function or sensory function (*e.g.*, movement of a limb) that is normally associated with neural activity at a "normal" location in the brain according to the functional organization of the brain. In several embodiments of the method 100, at least some neural activity related to the neural-function can be occurring at a site in the brain. The site of the neural activity may be at the normal location where neural activity typically occurs to carry out the neural-function according to the functional organization of the brain, or the site of the neural activity may be at a different location where the brain has recruited material to perform the neural activity. In either situation, one aspect of several embodiments of the method 100 is to determine the location in the brain where this neural activity is present.

The method 100 includes a diagnostic procedure 102 involving identifying a stimulation site at a location of the brain where an intended neural activity related to the neural-function is present. In one embodiment, the diagnostic

procedure 102 includes generating the intended neural activity in the brain from a “peripheral” location that is remote from the normal location, and then determining where the intended neural activity is actually present in the brain. In an alternative embodiment, the diagnostic procedure 102 can be performed by identifying a stimulation site where neural activity has changed in response to a change in the neural-function. The method 100 continues with an implanting procedure 104 involving positioning first and second electrodes at the identified stimulation site, and a stimulating procedure 106 involving applying an electrical current between the first and second electrodes. Many embodiments of the implanting procedure 104 position two or more electrodes at the stimulation site, but other embodiments of the implanting procedure involve positioning only one electrode at the stimulation site and another electrode remotely from the stimulation site. As such, the implanting procedure 104 of the method 100 can include implanting at least one electrode at the stimulation site. The procedures 102-106 are described in greater detail below.

Figures 2-4 illustrate an embodiment of the diagnostic procedure 102. The diagnostic procedure 102 can be used to determine the region of the brain where stimulation will likely effectuate the desired function, such as rehabilitating a loss of a neural-function caused by a stroke, trauma, disease or other circumstance. Figure 2, more specifically, is an image of a normal, healthy brain 200 having a first region 210 where the intended neural activity occurs to effectuate a specific neural-function in accordance with the functional organization of the brain. For example, the neural activity in the first region 210 shown in Figure 2 is generally associated with the movement of a patient’s fingers. The first region 210 can have a high-intensity area 212 and a low-intensity area 214 in which different levels of neural activity occur. It is not necessary to obtain an image of the neural activity in the first region 210 shown in Figure 2 to carry out the diagnostic procedure 102, but rather it is provided to show an example of neural activity that typically occurs at a “normal location” according to the functional organization of the brain 200 for a large percentage of people with normal brain function. It will be appreciated that the actual location of the first region 210 will generally vary between individual patients.

The neural activity in the first region 210, however, can be impaired. In a typical application, the diagnostic procedure 102 begins by taking an image of the brain 200 that is capable of detecting neural activity to determine whether the intended neural activity associated with the particular neural function of interest is occurring at the region of the brain 200 where it normally occurs according to the functional organization of the brain. Figure 3 is an image of the brain 200 after the first region 210 has been affected (*e.g.*, from a stroke, trauma or other cause). As shown in Figure 3, the neural activity that controlled the neural-function for moving the fingers no longer occurs in the first region 210. The first region 210 is thus “inactive,” which is expected to result in a corresponding loss of the movement and/or sensation in the fingers. In some instances, the damage to the brain 200 may result in only a partial loss of the neural activity in the damaged region. In either case, the image shown in Figure 3 establishes that the loss of the neural-function is related to the diminished neural activity in the first region 210. The brain 200 may accordingly recruit other neurons to perform neural activity for the affected neural-function (*i.e.*, neuroplasticity), or the neural activity may not be present at any location in the brain.

Figure 4 is an image of the brain 200 illustrating a plurality of potential stimulation sites 220 and 230 for effectuating the neural-function that was originally performed in the first region 210 shown in Figure 2. Figures 3 and 4 show an example of neuroplasticity in which the brain compensates for a loss of neural-function in one region of the brain by recruiting other regions of the brain to perform neural activity for carrying out the affected neural-function. The diagnostic procedure 102 utilizes the neuroplasticity that occurs in the brain to identify the location of a stimulation site that is expected to be more responsive to the results of an electrical, magnetic, sonic, genetic, biologic, and/or pharmaceutical procedure to effectuate the desired neural-function.

One embodiment of the diagnostic procedure 102 involves generating the intended neural activity remotely from the first region 210 of the brain, and then detecting or sensing the location in the brain where the intended neural activity has been generated. The intended neural activity can be generated by applying an input